the Denis et al patent. Accordingly, it would have been obvious to one of ordinary skill in the art at the time of applicant(s) invention having the Denis et al patent before him to regenerate or exfoliate the skin with a sugar phosphate such as galactose-6-phosphate in view of their analogous structure and the resulting expectation of similar therapeutic properties.

Applicants respectfully disagree with the Examiner's analysis of the teachings of the Denis patent, and its relevance to the present claims. If one reads beyond the teachings of the abstract, the document in question makes very clear that the sugar molecules in question are not utilized for their therapeutic value, but rather as a delivery system. Attention is drawn to the paragraph bridging columns 2 and 3, which refer to the discovery that "a product can be bound to the membrane of a keratinocyte by means of a ligand-receptor bond when using a product carry at least one ligand consisting of an oside residue". Clearly, the oside, one of which may be galactose-6-phosphate, are used in this context as the ligand, i.e., to bind the "product" having therapeutic value to a receptor site on the keratinocytes. The following paragraphs go on to disclose how to link the osides to the product, so that the product can be directly delivered to the keratinocyte. At column 6, lines 4 to 11, it is expressly noted that "the invention makes it possible toe achieve the cell targeting of a product, which can thus be concentrated specifically at the keratinocytes by virtue of the presence of at least one specific ligand consisting of an oside residue(emphasis added)". Thus, when the document is read in its entirety, it is clear that any beneficial effect achieved by the compositions disclosed therein are achieved by "the product" to which the ligand is bound, and not by the ligand *per se*, the sole function of which is to get the product to the proper cell. Indeed, all the formulas provided as examples of skin therapeutic compositions contain biologically active agents other than the osides, showing that the compositions are not relying on the osides for therapeutic activity. Therefore, one skilled in the art reading the Denis reference would not, under any circumstance, understand that galactose-6-phosphate has any therapeutic activity on skin, let alone exfoliation activity. Moreover, as the Examiner does recognize, exfoliation is not mentioned anywhere in the Denis document. The assertion that "exfoliation" encompasses "regeneration", which is mentioned is unsupported. The term "regeneration" can mean any number of things, for example healing of wounds or lesions, which is one of the activities specifically mentioned in Example 11, but which is not exfoliation. The Examiner is simply trying to make "exfoliation" be equivalent to "regeneration" in order to support a rejection that is otherwise unsupportable. For the reasons stated above, withdrawal of the rejection of claims 1, 2 and 5 is respectfully requested.

Claims 7, 8, 11, 13-15 and 18 have been rejected as being unpatentable over Denis et al, cited above. The rejection states as follows:

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> The Denis et al patent teaches a method for regeneration of the epidermis by application of a cosmetic or pharmaceutical composition that comprises α-D-galactose-6-phosphate...In the abstract, the Denis et al patent teaches the substitution of L-rhamnose with α-D-galactose-6-phosphate. See Example 10 of the Denis et al patent, which discloses an anti-wrinkle composition that comprises rhamnose and teaches an amount of rhamnose in the composition that embraces the amount of phosphosugar that is set forth in instant Claims 11 and 18. The instant claims differ from the Denis et al. patent by claiming that the application of a phosphosugar increases levels of glycosaminoglycans or is able to treat a skin condition associated with a reduced level of glycosaminoglycans in the skin. It is well establish[sic] in the prior art that beneficial results can be obtained by application of phosphosugars to the skin as demonstrated in the Denis et al patent. Applicants application of phosphosugar in methods to increase levels of glycosaminoglycans in the skin and to treat a skin condition associated with a reduced level of glycosaminoglycans in the skin is embraced by the method disclosed in the Denis et al patent since the regeneration of skin as described in the Denis et al patent suggests all the beneficial results associated with the revitalization of damage[sic]skin, which includes restoring the proper level of glycosaminoglycans to the skin. Accordingly it would have been obvious to one of ordinary skill in the art at the time of applicant(s) invention ...to regenerate or to normalized[sic] the level of glycosaminoglycans in skin by applying to the skin phosphosugars such as galactose-6-phosphate.

Again, Applicants must respectfully traverse this rejection. The arguments raised above with respect to claims 1, 2 and 5 apply equally here. As already unequivocally shown, no reasonable reading of the Denis document would suggest that galactose-6-phosphate had any skin therapeutic activity whatsoever: it is only used as a delivery system to bind the desired skin active to the keratinocytes. To take the misreading of the document one step further, the Examiner now asserts that it would have been obvious that these sugars could have the effect of increasing glycosaminoglycans, because the reference alludes to "regeneration of skin" as encompassing "all the beneficial results associated with revitalization of damage[d] skin". This is such a stretch of the imagination to infer such specific teachings from a single, simple generalization as to not merit serious argument in contravention. Is it the Examiner's position, then, that the teaching of "regeneration of skin" also encompasses the treatment of basal cell carcinoma, melanoma, Kaposi's sarcoma, ichthyosis, lichen planus, and the like? All of these exhibit "damaged skin" in some form or another; according to the Examiner's rationale, these would all be treatments that would be rendered obvious from the teachings of Denis as well. Clearly, such an expansive reading of the teachings of Denis is unjustified, and is simply being used, as it was above, to support a rejection for which no support can actually be found. The Examiner may not read intentions or effects into the prior art that are not there, and further, that would not be seen there by one of ordinary skill in the art. The simple fact is that the Examiner has not shown any teachings in this reference, or any other, that suggests to the skilled artisan that

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phosphosugars can enhance glycosaminoglycan levels, or in fact that they have any biological activity other than the ability to bind to a receptor on a keratinocyte. In the absence of any evidence of therapeutic activity of phosphosugars in Denis, the position that it would have been obvious to use same for any type of therapeutic activity, let alone the specific one claimed in the present claims, is insupportable, and the rejection should be withdrawn.

Claims 3, 4, 6, 9, 10, 12, 16, 17 and 19 have been rejected under 35 USC §103(a) as being unpatentable over Denis et al as applied above, and further in view of Ferguson, US Patent No. 5,520,926. The rejection states as follows:

> The Denis et al patent is applied to the instant rejection of the claims as disclosed in the above rejection of the claims under 35 USC 103. The instant claims differ from the Denis et al patent by reciting in the instant claims that the phosphosugar thereof is mannose-6-phosphate or mannose-1-phosphate. The Ferguson patent shows that the treatment of skin with mannose-6-phosphate and mannose-1-phosphate is well known in the art (see abstract). Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute the phosphosugar used in the Denis et al patent to regenerate skin with mannose-6-phosphate or mannose-1-phosphate, in view of the recognition in the art, as evidenced by the Ferguson patent, that mannose-6-phosphate or mannose 1-phosphate can effectively accelerate wound healing and mitigate scar formation of skin tissue.

The foregoing rejection cannot be supported on the record in the cited prior art. As has already been well-established, the Denis reference does not teach any therapeutic utility of a phosphosugar at all, so to the extent the rejection relies on Denis teaching "regeneration of skin", regardless of what that phrase may mean, with phosphosugars, it cannot be supported. Even if one assumes that the Examiner is correct in stating that it would be obvious to substitute the mannose phosphates of Ferguson for the phosphosugars disclosed in Denis et al., one would still not arrive at the present invention: one would only arrive at the conclusion that mannose phosphates could be used as ligands to deliver therapeutic products to the skin. On this basis alone the rejection fails. Moreover, the teachings of Denis would teach away from the substitution of the mannose phosphates for the galactose phosphate of Denis. Attention is drawn to the paragraph bridging columns 2 and 3 in Denis. The authors specifically note that the observed ligand effect is limited to the specific oside residues named, and even among the three named, they are not all of equivalent utility. Therefore, in view of the very specific teaching, combined with the teaching in Ferguson, in column 3, lines 15-19, stating that the mannose phosphates are not equivalent to galactose-6-phosphate, one skilled in the art would scarcely be led to substitute the mannose phosphates of Ferguson for the galactose-6-phopshate named by Denis, and even if he did, he would not achieve the methods of the present invention, as

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explained above. In the complete absence of any skin therapeutic utility for phosphosugars in Denis, and a completely different utility in Ferguson (prevention of scarring), there is simply no suggestion to be found in the prior art to use any phosphosugars, let alone a mannose phosphate phosphosugar to either exfoliate skin or to increase glycosaminoglycans in the skin. It is therefore requested that the rejection of claims 3, 4, 6, 9, 10, 12, 16, 17 and 19 be reconsidered an withdrawn.

CONCLUSION

The present claims are believed to be in condition for allowance, and prompt issuance of a Notice of Allowance is respectfully solicited. The Examiner is encouraged to contact the undersigned by telephone if it is believed that discussion will resolve any outstanding issues.

Respectfully submitted,

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